

CATALYTIC RNA AND SYNTHESIS OF THE PEPTIDE BOND

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The existence of catalytic RNA has suggested to some workers that in the earliest organisms RNA could have been both genetic material and catalyst. Although there are problems with current theories of how these organisms may have arisen, it is possible that translation was a relatively late invention by RNA organisms that already had evolved a considerable degree of biochemical complexity¹. The range of reactions that RNA is known to catalyze is limited, but it is possible that it once may have carried a greater variety of functional groups, and therefore may have been able to catalyze a greater variety of reactions. In collaboration with Tom Cech and Mike Yarus at the University of Colorado, Boulder, we are studying whether the L-19 IVS ribozyme from *Tetrahymena thermophila* can catalyze the formation of the peptide bond when it is supplied with synthetic aminoacyl oligonucleotides. If this reaction works, it could give us some insight into the mechanism of peptide bond formation and the origin of coded protein biosynthesis.

Two short oligoribonucleotides, CCCCC and a protected form of CCCC(U) were prepared; the former was made by the controlled hydrolysis of poly(C), and the latter by multistep chemical synthesis from the protected monomers. The homopentamer was then aminoacylated using ¹⁴C-labelled Boc-protected glycine imidazolide. This aminoacylated oligo-nucleotide has now been shown to enter the active site of the L-19 IVS, and aminoacyl transfer and peptide bond formation reactions are being sought. Our synthesis of CCCC(U) made us aware of the inadequacy of many of the 2'-hydroxyl protecting groups that are in use today and we therefore designed a new 2'-protecting group that is presently being tested.

1. S. A. Benner and A. D. Ellington, *Nature*, **329**, 295-6 (1987).